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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/873,601	06/12/97	NOLAN G	A-63915/DJB7

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EXAMINER	
GREEN, L.	
ART UNIT	**PAPER NUMBER**
1648	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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Office Action Summary	Application No. 08/873,601	Applicant(s) Nolan et al
	Examiner Green	Group Art Unit 1647

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 5/29/97.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-26 is/are pending in the application.

Of the above claim(s) 9-26 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-8 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

☐ Interview Summary, PTO-413

☒ Notice of References Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☒ Other Sequence rejections

Office Action Summary

Applicant's election without traverse of Group I in Paper No. 7 is acknowledged.

Claims 1-26 are pending, claims 9-26 stand withdrawn from consideration and claims 1-8 have been examined on their merits.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant must comply with these requirements in response to this office action. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Applicant is requested to return a copy of the attached Notice to Comply with the reply.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is indefinite in reciting " an exogenous precursor" as it is unclear of what the "precursor" is a precursor to.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1- 8 are rejected under 35 U.S.C. 102(e) as being anticipated by Khosla et al. (US 5,672,491).

Khosla et al. teach recombinant production of novel polyketides. This reference teaches that two general classes of polyketide synthases ("PKS") exist, with the type I PKSs including assemblies of several large multifunctional proteins, and is represented by the PKSs for macrolides such as erythromycin (see column 1, lines 59-64). This reference teaches that host cells lacking their native PKS gene cluster may be transformed with a replacement PKS gene cluster, which may be hybrid and include both type I and/or type II PKSs, and one may include as many genes as desired (see column 8). This reference teaches that 6-deoxyerythronolide B synthase (DEBS) catalyzed the biosynthesis of an erythromycin aglycone, and the polypeptides for DEBS are encoded in three open reading frames which are organized into modules, which also include an acyltransferase, β-ketoacyl carrier protein synthase, and others (see column 15, and Figure 9). Finally, this reference specifically exemplifies transformation of a *Streptomyces coelicolor* host cell with DEBS PKS genes (see column 27, Example 5). Thus, as this reference teaches that the type I PKSs including assemblies of several large multifunctional proteins, and is represented by

the PKSs for macrolides such as erythromycin, and specifically teaches a cell transformed with the DEBS PKS genes, which contains at a minimum 3 polypeptides, this reads on one of the polypeptides encoded by the open reading frames being the exogenous scaffold comprising at least a first binding site and a second binding site, with the other two polypeptides encoded by the other two open reading frames being the first and second enzymes, both heterologous to the cell, being bound to the binding sites of the first polypeptide. In addition, although this reference does not explicitly state, the other enzymes of the module, i.e. the an acyltransferase, β-ketoacyl carrier protein synthase, and others, are most likely associated with the complex, and would read on a scaffold having 3-5 binding sites, wherein the scaffold may be the same of different molecules. This would be an inherent property of the PKS complex encoded by the module.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bott et al. (WO 97/14789).

Bott et al. teach a composition comprising at least one enzyme which is bound to a peptide backbone, wherein said backbone is capable of having bound thereto a plurality of pre-selected enzymatic activities (see page 1). This reference teaches that in a preferred embodiment, a catalytic array will include one or several enzymes, the activity of which interacts together to create a synergistic effect. This reference teaches that the peptide backbone is a scaffolding protein which are characterized by a series of internal repeating elements, or scaffoldin domains, which comprise a means for non-covalently binding thereto an enzyme, wherein the enzyme would include a peptide sequence which facilitates binding, i.e. a "dockerin" (see page 6). This reference also teaches transformation of a host cell, which is transformed with an expression vector comprising the scaffoldin protein or the enzyme-dockerin protein(s), teaching that the host cells are capable of both replicating the expression vectors and expressing the desired product (see page 7). Bott et al. also teach that the invention includes a catalytic array wherein more than one enzyme, at least one of which is heterologous to the peptide backbone or dockerin segment, is non-covalently bound to the peptide backbone, allowing one to manipulate the conditions of the reaction to ensure that the catalytic array comprises a variety of enzymatic activities (see page 8). This reference fails to specifically exemplify a host cell transformed with both a scaffolding

protein and two or more enzymes containing a dockerin sequence, but it would have been obvious to one of ordinary skill in the art to do so in order to obtain a host cell which can catalyze a desired enzymatic reaction, which host cell can be replicated when desired and would express the entire catalytic array. The use of 3-5 or more binding sites on the scaffolding protein would have also been obvious in order to obtain a desired catalytic array, and it would have also been obvious to use different scaffolding protein, each with two or more binding sites, in order to achieve a desired catalytic reaction.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Ricard et al. teach that there is now experimental evidence that association of different enzymes as a multienzyme complex may result in alteration of the catalytic activities of the enzymes within the complex.

Khosla et al., WO 95/08548, is the published PCT, whose disclosure is basically the same as Khosla et al. (US 5,672,491).

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora M. Green, Ph.D. whose telephone number is (703) 308-3999.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Donald E. Adams, Ph.D., can be reached at (703)308-0570. The fax number for this art unit is (703)308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

LMG
8/14/98

LORA M. GREEN
PRIMARY EXAMINER

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